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09/756,899	01/09/2001	Franciscus Antonius, M. Redegeld	4692US	1305

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EXAMINER
HUYNH, PHUONG N

ART UNIT	PAPER NUMBER
1644	9

DATE MAILED: 07/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/756,899	Applicant(s) REDEGELD ET AL.
	Examiner " Neon" Phuong Huynh	Art Unit 1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/16/02; 1/9/01* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,10-13,16-25,31 and 32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,10-13,16-25,31 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Application/Control Number: 09/756,899

Art Unit: 1644

-DETAILED ACTION

1. Claims 1-5, 10-13, 16-25 and 31-32 are pending.

2. Applicant's election without traverse of Group I, claims 1-5, 10-13 and 16-25, (now claims 1-5, 10-13, 16-25, and 31-32) drawn to a compound that inhibits the binding of the free light chain of immunoglobulin, filed 4/16/02, is acknowledged.

3. Claims 1-5, 10-13, 16-25, and 31-32 are being acted upon in this Office Action.

4. The international reports crossed out on PTO 1449 filed 1/9/01 have been considered.

5. The drawings, filed 1/9/01, are not approved. Please see enclosed PTO 948, Notice of Draftsperson's Patent Drawing Review. Appropriate action is required.

6. The disclosure is objected to because of the following informality: "Ic LC" on page 7, line 14 should have been "Ig LC". Appropriate action is required.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-5, 10-13, 16-25 and 31-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) a compound wherein the compound is a peptide consisting of SEQ ID NO: 1 that inhibits the binding of free light chain of immunoglobulin (LC) to mast cells *in vitro* wherein when said peptide is in the presence of an equimolar quantity of the free light chain of immunoglobulin in a solution, the free light chain of immunoglobulin's binding to said mast cells is reduced by at least 5% for inhibiting the binding of free light chain of immunoglobulin, (2) the said peptide also binds to the free light chain of immunoglobulin; competes with a peptide for binding to the free light chain of immunoglobulin *in vitro*, wherein said peptide has the amino acid sequence AHWSGHCCL (SEQ ID NO: 1) and wherein when said compound and said peptide are present in equimolar amounts in a solution, said peptide

reduces binding of said peptide to said free light chain of immunoglobulin by at least 5% or 10%, (3) the said compound reduces the binding of said peptide to the free light chain of immunoglobulin by at least 25%, 50%, 75% or 90% *in vitro*, (4) the said compound has a mass of less than 10 kDal, or 2 kDal and inhibits the binding of free light chain of immunoglobulin (LC) to mast cells *in vitro*, (5) a compound wherein the compound is a peptide consisting of SEQ ID NO: 1 produced by the process recited in claim 22 wherein said compound has a mass less than 10 kDal or a mass less than 2 kDal, and the said compound is an LC-binding peptide fragment of Tamm-Horsfall glycoprotein for inhibiting the binding of free light chain of immunoglobulin (LC) to mast cells *in vitro*, **does not** reasonably provide enablement for (1) *any* compound that inhibits binding of free light chain of immunoglobulin (LC) to mast cells: wherein when the compound is in the presence of an equimolar quantity of the free light chain of immunoglobulin in a solution, the free light chain of immunoglobulin's bindings to said mast cells is reduced by at least 5%, (2) *any* compound binds to the free light chain of immunoglobulin; competes with a peptide for binding to the free light chain of immunoglobulin, wherein said peptide has the amino acid sequence AHWSGHCCL (SEQ ID NO: 1) and wherein when said compound and said peptide are present in equimolar amounts in a solution, said compound reduces binding of said peptide to said free light chain of imunoglobulin by at least 5%, (3) *any* compound mentioned above wherein the compound reduces the binding of said peptide to the free light chain of immunoglobulin by at least 10%, (4) *any* compound mentioned above wherein the compound is *any* peptidedomimeticum, (5) *any* compound mentioned above wherein the compound is a pharmaceutically acceptable compound, (6) *any* compound for treating *any* disease state in a subject, said disease state characterized by exhibiting: (i) a serum concentration of free light chain of immunoglobulin in serum of at least 8 mg/ml; (ii) a spinal fluid concentration of free light kappa-chain of immunoglobulin of at least 70 μg/l and/or (iii) a spinal fluid concentration of free lamda-chain of immunoglobulin of at least 300 μg/l; said compound comprising wherein when the compound is in the presence of an equimolar quantity of free light chain of immunoglobulin (LC), reduces the equimolar quantity of LC's binding to mast cells present in solution therewith by at least 5%, (7) *any* compound mentioned above wherein the compound inhibits LC's binding to mast cells present in solution by at least 10%, (8) *any* compound mentioned above wherein the disease is selected from the group consisting of chronic inflammatory bowel disorders, viral injection and multiple sclerosis, (9) *any* pharmaceutical composition comprising *any* compound mentioned above that in the presence of an equimolar quantity of free light chain of

immunoglobulin (LC), reduces the equimolar quantity of LC's binding to mast cells present in the solution by at least 5%, with a pharmaceutically acceptable carrier or diluent, (10) *any* compound mentioned above wherein the compound reduces the binding of said peptide to the free light chain of immunoglobulin by at least 25%, 50%, 75%, or 90%, (11) *any* peptidomimeticum compound mentioned above wherein the compound has a mass less than 10 kDal, or 2kDal, (12) *any* compound produced by a process comprising screening a series of compounds wherein said screening comprising (a) incubating *any* compound from a series of compounds with an admixture comprising LC and *any* labeled compound, said labeled compound comprising *any* compound and a label and said compound capable of i) binding the free light chain of immunoglobulin, and ii) competing with a peptide with the amino acid sequence of SEQ ID NO: 1 for binding with the free light chain of immunoglobulin and isolate the compounds which bind LC and compete with the peptide, (13) any compound produced by said process characterized in that has a mass less than 10 kDal, is *any* LC-binding peptide fragment of Tamm-Horsfall glycoprotein or *any* derivative thereof, (14) *any* pharmaceutical composition mentioned above wherein the compound binds LC; competes for binding with LC and a peptide with the amino acid sequence AHWSGHCCL (SEQ ID NO:1) and reduces binding of said peptide with LC by at least 5% when said compound and said peptide are present in a solution with said LC in equimolar amounts, and (15) *any* pharmaceutical composition mentioned above wherein the compound is *any* peptide having a mass of less than 10 kDal for treating any disease such as asthma, allergy, chronic inflammatory bowel disorders, viral infection, and multiple sclerosis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only three peptides selected from the group consisting of SEQ ID NO: 1-3 and only peptide consisting of SEQ ID NO: 1 at 0.25mg/ml and 0.5 mg/ml can inhibit free light chain of Ig binding to mast cells (See page 8, and Fig 1 of the specification). The specification also discloses that TNP specific Ig light chain but not the Ig heavy chain and mast cell are important in sensitization of mice to antigen such as PSA (See page 9-10 Table 1, 2 and 3 of the specification). The specification further discloses that immunoglobulin light chain also binds to human uromodulin, which is a Tamm-Horsefall glycoprotein (THP) (See page 11 of the specification).

The specification does not teach how to make and use *any* "compound" *any* "peptide fragment" of Tamm-Horsefall glycoprotein, and *any* "derivative thereof" mentioned above for inhibiting Ig light chains binding to mass cells or for treating any disease such as asthma, allergy, chronic inflammatory bowel disorders, viral infection and multiple sclerosis. There is no guidance and working example in the specification as filed that preventing the interaction of Ig light chain binding to mast cells using *any* compound, *any* peptide fragment of Tamm-Horsfall glycoprotein or *any* derivative thereof mentioned above, including SEQ ID NO: 1, will unequivocally reduce sensitization, in turn, would be useful for treating disease such as asthma, allergy, chronic inflammatory bowel disorders, viral infection and multiple sclerosis. The term "compound" can be *any* peptide, *any* polypeptide, *any* nucleic acid, *any* organic molecule, *any* DNA, or *any* RNA. There is no structure associated with function for the term "compound". The specification discloses only three peptides consisting of SEQ ID NO: 1-3. Further, only peptide consisting of SEQ ID NO: 1 inhibits the binding of Ig light chain to mast cells *in vitro*. Given the indefinite number of undisclosed "compound", it is unpredictable which undisclosed compound will inhibit the binding of free light chain of immunoglobulin to mast cell, in turn, would be useful for treating just any disease such as the ones mentioned above.

Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (See Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). Given the lack of guidance and working examples, predicting what changes can be made to the undisclosed compound or peptide that after substitution, deletion, insertion and/or modification will retain both structure and have similar function as peptide of SEQ ID NO: 1 is unpredictable.

Further, there are insufficient in vivo working examples that *any* compound mentioned above could treat just any disease such as asthma, allergy, chronic inflammatory bowel disorders, viral infection and multiple sclerosis.

Redegeld *et al* teach that currently no pathophysiological role for secreted IgLCs has been documented. Free light chain immunoglobulin does not activate gamma chain of the Fcγ chain associated with the Fc receptors such as FcεRI, and FcγRIII, which are expressed on mast cell. IgLC mediated mast cells is independent of complement activation. Redegeld *et al* further teach IgLC antagonist such as F991, which is a 9mers peptide (AHWSGHCCL) can prevent hapten-induced ear swelling, which is contact delayed hypersensitivity reaction. Given that currently no pathophysiological role for secreted IgLCs has been documented, it is not predictable which undisclosed compound would be effective in treating any disease such as the ones mentioned above. A pharmaceutical composition in the absence of in vivo data are unpredictable for the following reasons; (1) the compound such as peptide may be inactivated before producing an effect, i.e. such as proteolytic degradation; (2) the compound such as peptide may not reach the target area because, i.e. the peptide may not be able to stay in circulation or target to elsewhere or where the peptide has no effect; and (3) other functional properties, known or unknown, may make the peptide unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992). Without knowing the specific structure of undisclosed compound, "peptide fragment" of Tamm-Horsefall glycoprotein, "derivative thereof" and not to mentioned peptidomimeticum of *any* undisclosed compound, it is unpredictable which undisclosed compound, peptide fragment and derivative thereof would be useful for inhibiting the binding of free light chain immunoglobulin to mast cells, in turn, for treating just *any* disease. Even if the compound wherein the compound is a peptide consisting of SEQ ID NO: 1 is disclosed and has demonstrated that it prevents the binding of free light chain immunoglobulin to mast cells *in vitro*, neither the circumstantial evidence nor the art teach that preventing the interaction of Ig light chain with mast cell would unequivocally reduce sensitization to any allergen, in turn, useful for treating asthma, let alone treating inflammatory bowel disease, viral infection, and multiple sclerosis. Further, given that the claimed compound has to be in equimolar amounts in a solution in order to reduce the binding of the free light chains to mast cells even in vitro only by 5% when in vivo mast cells are usually reside in tissues and very heterogeneous in nature, it is not obvious how any compound when in equimolar concentration as

the free light chains of the immunoglobulin in serum at least 8 mg/l, or in spinal fluid concentration of at least 70 μg/l and or in spinal fluid at least 300 μg/l would be effective for treating any disease in a subject such as viral infection and multiple sclerosis since free light chain immunoglobulin does not even activate gamma chain of the Fcγ chain associated with the Fc receptors such as FcεRI, and FcγRIII that are expressed on mast cell as taught by Redegeld *et al* discussed supra.

Van Noort *et al* teach that models of autoimmune diseases depends on numerous factors such as animal strains used, the antigens used, the immunization protocol used, especially some protocol for EAE that result in a single acute episode while others induce chronic relapsing disease (See page 168-169, in particular). Van Noort *et al* teach that induction of EAE with MBP does not result in the development of relapse and the clinical course may be different than that after treatment with other antigen such as SCH and PLP (See page 170, in particular). Given the indefinite number of autoimmune diseases that differ with respect to animal strains used, the antigens used, the immunization protocol used in light of the teaching of the specification with respect to inhibiting the binding of immunoglobulin light chain to mast cell in the literature, it would take undue amount of experimentation to practice the claimed invention. Given the undisclosed compound is not enabled, it follows that any compound that reduces the binding of *any* peptide to the free light chain of immunoglobulin by at least 25%, 50% 75% or 90% is not enabled. It also follows that any undisclosed compound that has a mass of less than 10 kDal or 2 kDal is not enabled.

With regard to claim 22, there is insufficient guidance and lack of working examples for screening compound or any compound produced by a process recited in claim 22 where the screening process comprising incubating any compound with an admixture comprising LC and any labeled compound, said labeled compound comprising any compound and any label and said compound is capable of binding the free light chain of immunoglobulin and competing with a peptide (SEQ ID NO: 1) for binding to the free light chain and isolating the compounds which bind LC and complete with the peptide. Further, the compound is any LC-binding peptide fragment of Tamm-Horsfall glycoprotein or any derivative thereof, there is insufficient guidance and working example as to which undisclosed peptide fragment of Tamm-Horsfall glycoprotein is capable of binding to LC. There is no structure (amino acid residues) associated with the term "peptide fragment". Given the indefinite number of undisclosed LC-binding peptide fragment, it is unpredictable which undisclosed peptide fragment of Tamm-Horsfall glycoprotein would bind

to LC. Since the LC-binding peptide fragment is not enabled, it follows that any derivative thereof is not enable.

For these reasons, it would require undue experimentation even for one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992). In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

9. Claims 1-5, 10-13, 16-25 and 31-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) *any* compound that inhibits binding of free light chain of immunoglobulin (LC) to mast cells: wherein when the compound is in the presence of an equimolar quantity of the free light chain of immunoglobulin in a solution, the free light chain of immunoglobulin's bindings to said mast cells is reduced by at least 5%, (2) *any* compound binds to the free light chain of immunoglobulin; competes with a peptide for binding to the free light chain of immunoglobulin, wherein said peptide has the amino acid sequence AHWSGHCCL (SEQ ID NO: 1) and wherein when said compound and said peptide are present in equimolar amounts in a solution, said compound reduces binding of said peptide to said free light chain of imunoglobulin by at least 5%, (3) *any* compound mentioned above wherein the compound reduces the binding of said peptide to the free light chain of immunoglobulin by at least 10%, (4) *any* compound mentioned above wherein the compound is *any* peptidedomimeticum, (5) *any* compound mentioned above wherein the compound is a pharmaceutically acceptable compound, (6) *any* compound for treating *any* disease state in a subject, said disease state characterized by exhibiting: (i) a serum concentration of free light chain of immunoglobulin in serum of at least 8 mg/ml; (ii) a spinal fluid concentration of free light kappa-chain of immunoglobulin of at least 70 µg/l and/or (iii) a spinal fluid concentration of free lamda-chain of immunoglobulin of at least 300 µg/l; said

compound comprising wherein when the compound is in the presence of an equimolar quantity of free light chain of immunoglobulin (LC), reduces the equimolar quantity of LC's binding to mast cells present in solution therewith by at least 5%, (7) *any* compound mentioned above wherein the compound inhibits LC's binding to mast cells present in solution by at least 10%, (8) *any* compound mentioned above wherein the disease is selected from the group consisting of chronic inflammatory bowel disorders, viral injection and multiple sclerosis, (9) *any* pharmaceutical composition comprising *any* compound mentioned above that in the presence of an equimolar quantity of free light chain of immunoglobulin (LC), reduces the equimolar quantity of LC's binding to mast cells present in the solution by at least 5%, with a pharmaceutically acceptable carrier or diluent, (10) *any* compound mentioned above wherein the compound reduces the binding of said peptide to the free light chain of immunoglobulin by at least 25%, 50%, 75%, or 90%, (11) *any* peptidomimeticum compound mentioned above wherein the compound has a mass less than 10 kDal, or 2kDal, (12) *any* compound produced by a process comprising screening a series of compounds wherein said screening comprising (a) incubating *any* compound from a series of compounds with an admixture comprising LC and *any* labeled compound, said labeled compound comprising *any* compound and a label and said compound capable of i) binding the free light chain of immunoglobulin, and ii) competing with a peptide with the amino acid sequence of SEQ ID NO: 1 for binding with the free light chain of immunoglobulin and isolate the compounds which bind LC and compete with the peptide, (13) any compound produced by said process characterized in that has a mass less than 10 kDal, is *any* LC-binding peptide fragment of Tamm-Horsfall glycoprotein or *any* derivative thereof, (14) *any* pharmaceutical composition mentioned above wherein the compound binds LC; competes for binding with LC and a peptide with the amino acid sequence AHWSGHCCL (SEQ ID NO:1) and reduces binding of said peptide with LC by at least 5% when said compound and said peptide are present in a solution with said LC in equimolar amounts, and (15) *any* pharmaceutical composition mentioned above wherein the compound is *any* peptide having a mass of less than 10 kDal for treating any disease such as asthma, allergy, chronic inflammatory bowel disorders, viral infection, and multiple sclerosis.

The specification discloses only three peptides selected from the group consisting of SEQ ID NO: 1-3 and only peptide of SEQ ID NO: 1 at 0.25mg/ml and 0.5 mg/ml can inhibit free light chain of Ig binding to mast cells (See page 8, and Fig 1 of the specification). The specification also discloses that TNP specific Ig light chain but not the Ig heavy chain and mast cell are

important in sensitization of mice to antigen such as PSA (See page 9-10 Table 1, 2 and 3 of the specification). The specification further discloses that immunoglobulin light chains also binds to human uromodulin, which is a Tamm-Horsefall glycoprotein (THP) (See page 11 of the specification).

With the exception of the specific compound mentioned above, there is insufficient written description about the structure associated with function of *any* compound that inhibits binding of free light chain of immunoglobulin (LC) to mast cells, *any* pharmaceutical composition comprising *any* compound, *any* compound is *any* LC-binding peptide fragment of Tamam-Horsfall glycoprotein or *any* derivative thereof. The specification discloses only **one** working peptide consisting of SEQ ID NO: 1 that inhibits the binding of free light chain of immunoglobulin to mast cells *in vitro*. Given the lack of any additional compound that can inhibit the binding of free light chain of immunoglobulin to mast cells, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

11. Claims 22-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "labeled compound" in claim 22 line 5 and "compound" claim 22 line 6 is indefinite and ambiguous. As written, it is not clear the claimed compound or the labeled compound is capable of binding to the free light chain of immunoglobulin and competing the with peptide of SEQ ID NO: 1 for binding to the free light chain of immunoglobulin. One of ordinary skilled in the art cannot appraise the metes and bound of the claimed invention. Appropriate correction is required.

12. Claims 1-5, 10-13, 16-25 and 31-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Huang *et al* (J Clin Invest 99(4): 732-36, 1997; PTO 1449).

Huang *et al* teaches various compound such as a synthetic peptide AHWSGHCCL produced by a process comprising screening a series of compounds for it's capability to bind to an immunoglobulin light chain (LC) (See Methods, Table 1, page 734, in particular). The reference peptide is identical to the claimed compound. The reference compound is also identical to the claimed peptide of SEQ ID NO: 1, which has the amino acid sequence AHWSGHCCL for binding with the free light chain of immunoglobulin. The reference compound can reduce the binding of the claimed peptide AHWSGHCCL with immunoglobulin light chain (LC) by 50 %, which is at least 5%, at least 10% at least 25% when the reference compound and reference peptide are present in equimolar amounts (See Table 1 mic, IC_{50} mM, in particular). The reference compound AHWSGHCCL is an LC-binding peptide fragment of Tamm-Horsfall glycoprotein, which is also a derivative of Tamm-Horsfall glycoprotein. The reference compound inherently has a mass less than 10 kDal or less than 2 kDa since the sum of the molecular weight of each of the amino acids (87+155+204+105+75+155+121+121+131) is about 1.15 kDal. Since the reference compound is the same as the claimed compound, it inherently inhibits the binding of free light chain of immunoglobulin (LC) to mast cells when the reference compound is in the presence of an equimolar quantity of the free light chain of immunoglobulin in a solution by at least 5%, and the reference compound competes with the claimed peptide having the amino acid sequence AHWSGHCCL of SEQ ID NO: 1 to reduced the binding of the claimed peptide to the free light chain by at least 75% and at least 90%. Claims 10 and 12 are included in this rejection because the inherently properties of the reference compound is capable of treating a disease such as the ones recited in claim 12 characterized by exhibiting a serum concentration of free light chain of immunoglobulin in serum at least 8 mg/ml or a spinal fluid concentration of free light chain of at least 70 μg/l and/or a spinal fluid concentration of free lambda chain of immunoglobulin of at least 300 μg/l and reduces LC's binding to mast cells when the reference compound is in the presence of an equimolar quantity of free light chain of immunoglobulin. Claims 13 and 31 are included in this rejection because the reference teaches a pharmaceutical composition comprising the reference compound and a solution such as PBS, which is a pharmaceutical acceptable carrier or diluent (See page 733, column 1, second paragraph, in particular). Thus, the reference teachings anticipate the claimed invention.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

15. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
July 1, 2002

Christina Chan

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